



UNITED STATES DEPARTMENT OF COMMERCE
Patent and Trademark Office

Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231

| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. |
|-----------------|-------------|----------------------|---------------------|
| 09/315,298 | 05/20/99 | TENG | C ISIS-3510 |

HM12/0314

MICHAEL P STRAHER
WOODCOCK WASHBURN KURTZ MACKIEWICZ
& NORRIS LLP
ONE LIBERTY PLACE 46TH FLOOR
PHILADELPHIA PA 19103

EXAMINER

EPPS, J

ART UNIT

PAPER NUMBER

1635

DATE MAILED: 03/14/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.

09/315,298

Applicant(s)

TENG ET AL.

Examiner

Janet L Epps

Art Unit

1635

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on 18 December 2000.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-7, 9-20, 46-66, 80 and 83 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-7, 9-20, 46-66, 80 and 83 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

- 15) ☒ Notice of References Cited (PTO-892)
- 16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 17) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____
- 18) ☐ Interview Summary (PTO-413) Paper No(s) _____
- 19) ☐ Notice of Informal Patent Application (PTO-152)
- 20) ☐ Other: _____

DETAILED ACTION

1. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.
2. Claims 1-7 and 9-10 remain rejected under 35 USC 102(b) as anticipated by Narayanan et al. for the reasons of record in the Official Action mailed 9-12-2000.

Applicant's arguments filed 12-10-2000 have been fully considered but they are not persuasive. Applicants traverse this rejection on the grounds that the Narayanan patent does not disclosed penetration enhancers. The specification as filed describes penetration enhancers "facilitate the transport of drug molecules, for example, oligonucleotides an other nucleic acids, across mucosal and other epithelial membranes (specification, page 8, lines 4-15). Contrary to Applicant's assertions, the compositions of Narayanan et al. may comprise oligomers associated with targeted carriers such as antibody or receptor fragments, ligand molecules, hormones, and enzymes or may be provided in liposomes or micelles for more efficient delivery into cells. Thus, Narayanan et al. disclose penetration enhancers that are useful in facilitating the transport of oligomers into cells (col. 5, lines 45-66).

3. Claims 80 and 83 remain rejected, and claims 1-7, 19-20, 46-64 are rejected under 35 U.S.C. 102(e) as being anticipated by Bennett et al. (US 6,111,094A1), for the reasons of record in the Official Action mailed 9-12-2000.

Applicant's arguments filed 12-18-2000 have been fully considered but they are not persuasive. Applicants traverse by way of amendment cancelling



claims 81 and 82. Additionally, Applicants argue that since claims 80 and 83 depend on claims 1 and 46, the Bennett patent does not anticipate these claims.

However, Bennett et al. clearly discloses pharmaceutical compositions comprising an antisense oligonucleotide, wherein said composition further comprises a microemulsion, a penetration enhancer, a bile salt, a chelating agent, a surfactant, or a carrier compound. In addition, the oligonucleotides according to SEQ ID NO: 1 and 55 are clearly disclosed as ISIS 2302 of the Bennett et al. invention. The instant claims remain rejected as anticipated by Bennett et al.

4. Claims 7 and 9-18 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 7 recites "wherein said microemulsion is selected from the group consisting of an oil-in-water microemulsion, a water-in-oil microemulsion, an oil-in-water-in-oil microemulsion a water in-oil-in-water microemulsion. This claim appears to recite a Markush group without the proper use of the Markush format. Alternative expressions are permitted if they present no uncertainty or ambiguity with respect to the question of scope or clarity of the claims. One acceptable form of alternative expression, which is commonly referred to as a Markush group, recites members as being "selected from the group consisting of A, B and C." See *Ex parte Markush*, 1925 C.D. 126 (Comm'r Pat. 1925).

Claims 9-18 all depend from a cancelled base claim. Claim 8 was cancelled by the amendment filed 12-18-2000.

5. Claims 46 and 65-66 are rejected under 35 U.S.C. 102(e) as being anticipated by Wong et al. (see entire document)

The instant claims read on a composition comprising an oligonucleotides in oral dosage form, further comprising a plasticizer.

Wong et al. disclose formulations for oral dosage, wherein said formulation may comprise antisense oligonucleotides (col. 19, line 46, and plasticizers such as polyhydric alcohols, polyethylene glycol, glycerol, propylene glycol, acetate esters, glycerol triacetate, triethyl citrate, acetyl triethyl citrate, glycerides, acetylated monoglycerides, oils, mineral oil, and castor oil (col. 14, lines 7-14).

Wong et al. teach each and every aspect of the instant invention thereby anticipating Applicant's claimed invention.

6. Claims 46, 52-53, 56-57 and 59-61 are rejected under 35 U.S.C. 102(e) as being anticipated by New et al. (see entire document)

New et al. disclose formulations in oral dosage form (col. 1, lines 5-9) comprising a biologically active material, wherein said biologically active materials may also be oligonucleotides such as antisense oligonucleotides and their analogues (col. 7, lines 5-12), and a adsorption or penetration enhancer such as a bile salt (col. 3, lines 37-48). The bile salts of New et al. comprise both ursodeoxycholic acid and chenodeoxycholic acid. Additionally, the

compounds of New et al. may also further comprise a chelator molecules such as EDTA or ethylene glycol (col. 6, lines 35-41), and comprise an enteric coating (tablet form) to prevent dissolution in the stomach (col. 7, lines 36-50).

New et al. teach each and every aspect of the instant invention thereby anticipating Applicant's claimed invention.

7. Claims 1-7, 9- 20, and 46-62 are rejected under 35 U.S.C. 102(e) as being anticipated by McKay et al. (see entire document)

McKay et al. disclose compositions comprising antisense oligonucleotides, wherein said antisense oligonucleotides may comprise 2' sugar modifications including, e.g. SH, SCH₃, F, and -OCH₃CH₃ (col. 8, lines 40-63). The compositions of McKay et al. are suitable for oral administration and may be presented as discrete units such as capsules, cachets or tablets each containing predetermined amounts of the active ingredients; as powders or granules; as solutions or suspensions in an aqueous liquid or a non-aqueous liquid; or as oil-in-water emulsions or water-in-oil liquid emulsions. Additionally, these compositions may comprise penetration enhancers, which may be classified as belonging to one of five broad categories, i.e., fatty acids, bile salts, chelating agents, surfactants and non-surfactants. Various fatty acids and their derivatives which act as penetration enhancers include, for example, oleic acid, lauric acid, capric acid, myristic acid, palmitic acid, stearic acid, linoleic acid, linolenic acid, dicaprinate, tricaprinate, ricinoleate, monoolein. Surfactants of this invention include (*inter alia*) polyoxyethylene-9-lauryl ether (col. 22, lines 5-67).


McKay et al. teach each and every aspect of the instant invention thereby anticipating Applicant's claimed invention.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Janet L Epps whose telephone number is 703-308-8883. The examiner can normally be reached on Mondays through Friday, 9:00AM to 6:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John LeGuyader can be reached on (703)-308-0447. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-305-7939 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

JLE
February 28, 2001


ROBERT A. SCHWARTZMAN
PRIMARY EXAMINER